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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/524,459	03/10/2000	George Liang King	10276-026001	5799

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FISH & RICHARDSON PC
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EXAMINER

JONES, DWAYNE C

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 06/18/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/524,459

Applicant(s)

KING, GEORGE LIANG

Examiner

Dwayne C Jones

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 9-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 6-8 is/are allowed.
- 6) ☐ Claim(s) 1-5 and 9-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Status of Claims

1. Claims 1-3 and 5-15 are pending.
2. Claims 16 and 18-29 were cancelled in the amendment of February 5, 2003.
3. Claims 1-3 and 5 are rejected.
4. Claims 6-8 are allowable.

Response to Arguments

5. Applicant's arguments filed February 5, 2003 have been fully considered but they are not persuasive with respect to the scope of enablement rejection under 35 U.S.C. 112, first paragraph for claims 1-3 and 9-15. Applicants make the following arguments for the scope of enablement rejection. First, applicants asserts that the prior art reference of Goekjian et al. provide examples of inhibitors of PKC.
6. Applicant first asserts that the prior art reference of Goekjian et al. provide examples of inhibitors of PKC. The instant specification does not teach nor provide guidance that all inhibitors of PKC are effective in treating permeability failure. In fact, the instant specification only provides guidance for the PKC inhibitors of First, applicants asserts that the prior art reference of Goekjian et al. provide examples of inhibitors of PKC bisindolylmaleimide and LY333531 as well as vitamin E. A skilled artisan would only choose inhibitors of PKC that are structurally related to inhibitors of PKC bisindolylmaleimide, LY333531, and vitamin E to treat permeability failure.

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7. Applicant argues that the instant claims are free of a written description rejection under 35 U.S.C. 112, first paragraph for claims 1-3 and 9-15 in the arguments filed February 5, 2003. Even though this rejection was not made in the office action of July 30, 2002 applicant's arguments were considered but they were not persuasive for the following reasons.

8. Claims 1-5 and 9-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant independent claim 1 is directed to a method of treating permeability failure in a subject, comprising introducing into said subject a peritoneal dialysis fluid, which includes a specific inhibitor of a PKC, thereby treating said subject. This independent claim as well as dependent claims 2, 3, and 5 fail to meet the written description requirement for the following reasons. The term a specific inhibitor of PKC, as well as the terms of dependent claims 2, 3 and 5, namely a specific inhibitor of PKC beta, and a specific inhibitor of PKC beta, a specific inhibitor of PKC gamma, and a specific inhibitor of PKC delta, are written functionally. There is insufficient descriptive support for these functional terms in the instant specification. Moreover, the instant specification does not describe what is meant by the functional characteristics of being known as a specific inhibitor of PKC beta, a specific inhibitor of PKC beta 1, a specific inhibitor of PKC gamma, and a specific inhibitor of PKC delta. Structural identifying characteristics of being known as a specific

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inhibitor of PCK beta, beta 1, gamma or delta are not disclosed. There is no evidence that there is any per se structure/function relationship between the disclosed term of a specific inhibitor of PCK beta, beta 1, gamma or delta and any others that might be found using the claimed method. Furthermore, there is no support that the particularly disclosed terms of a specific inhibitor of PCK beta, gamma or delta are represented by the sole examples of bis(indolyl)maleimide or LY333531. The specification does; however, provide an adequate written description of the term specific inhibitor of PKC for the structural compounds of bis(indolyl)maleimide or LY333531 or vitamin E.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-5 and 9-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons stated above in paragraphs nos. 7 and 8.

11. Claims 1-5 and 9-15 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the PKC inhibitors of bisindolylmaleimide, LY333531, or vitamin E, does not reasonably provide enablement

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for other types of PKC inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to a method of treating permeability failure in a subject by using a peritoneal dialysis fluid, which includes a specific inhibitor of PKC. The method comprises administering a peritoneal dialysis fluid, which includes a specific inhibitor of PKC in order to treat permeability failure in a subject.

(2) The state of the prior art

The compounds of the inventions are inhibitors of PKC.

(3) The relative skill of those in the art

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The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotrophic hormones was unpredictable art); In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of inhibitor of PKC prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claim 1 is directed to the plethora of compounds that are embraced by the functional description of being known as inhibitors of PKC. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.), cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires

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more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of an inhibitor of PKC to be effective in treating permeability failure is insufficient for enablement. The specification provides no guidance, in the way of enablement for inhibitors of PKC other than bis(indolyl)maleimide, LY333531, or vitamin E. The specification provides no guidance, in the way enablement for other types of inhibitors of PKC other than bis(indolyl)maleimide, LY333531, or vitamin E. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim

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will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses inhibitors of PKC that are use to treat permeability failure. However, the instant specification only has enablement for bis(indolyl)maleimide, LY333531, or vitamin E.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the compounds that are known by the functional terminology of the generic phrase PKC inhibitors that would be enabled in this specification.

Allowable Subject Matter

12. Claims 6-8 are allowed.

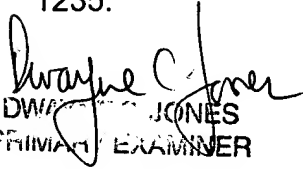
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (703) 308-4634. The examiner can normally be reached on Mondays through Fridays from 8:30 am to 6:00 pm. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-

1235.


DWAYNE C. JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
June 13, 2003